



REMARKS

Entry of this Submission and reconsideration of the subject application in view thereof are respectfully requested.

Applicant respectfully submits that the record including the Submission under 37 C.F.R. § 1.114 filed with the Office on November 7, 2011 makes it clear that the Examiner has not established a *prima facie* case of anticipation based on Toby or of obviousness based on Toby and Manfredi.

In addition, Applicant submits herewith a sworn declaration by Dr. Andreas Burkovski (attached as **Exhibit A**) ("Burkovski declaration") in support of its arguments of record in the Amendment and Response filed with the Office on July 28, 2010 and November 7, 2011. By presenting the Burkovski declaration, Applicant has conclusively established that the claimed method for monitoring the expression level of a gene in a host cell by modulating the activity of a regulatory biomolecule is neither anticipated by Toby, nor obvious over Toby and Manfredi.

Dr. Burkovski is a Microbiology Professor and the Chair of Microbiology at Friedrich-Alexander University Erlangen-Nuremberg, the Applicant for the above-referenced application. Dr. Burkovski is specialized in physiology and biotechnology of various microorganisms. Dr. Burkovski's testimony is based on his first-hand, personal knowledge of physiology and regulation of microorganisms at different cellular levels generally and his understanding of the protein-protein interactions of the type disclosed in Toby. A declaration is, itself, evidence, and the declaration by Dr. Burkovski refutes the Examiner's unsupported contentions. As such, Dr. Burkovski's declaration is authoritative and is sufficient to overcome the rejections based on Toby, and Toby and Manfredi.

Specifically, with respect to the anticipation rejection based on Toby, Dr. Burkovski disagrees with the Examiner and testifies in paragraphs 9-14 that Toby is not sufficient to anticipate the rejected claims. Dr. Burkovski testifies that there are material differences between yeast two-hybrid methods taught in Toby and the claimed method. Toby does not disclose the limitations in claim 1(a)(ii). For example, Toby's two-hybrid method requires constant binding of the bait to the DNA to allow reporter gene readout. The method claimed in the present application requires the exact opposite, which requirement is the regulation of the nucleic acid binding activity of the bound bait protein in order to allow reporter gene readout. See paragraphs

11 and 12 of Burkovski declaration. Toby also fails to disclose the limitations set forth in claim 1(b). See paragraph 13 of Burkovski declaration. Dr. Burkovski also testifies in paragraph 14 of his declaration that Toby is not an enabling reference. Therefore, in Dr. Burkovski's opinion, Toby does not anticipate the rejected claims.

With regard to the rejection of claim 6 as obvious over Toby and Manfredi, Dr. Burkovski expresses his opinion in paragraph 18 that the combination of Toby and Manfredi does not render claim 6 obvious. In particular, Dr. Burkovski testifies that Toby's teachings about yeast two-hybrid systems do not even remotely suggest, either explicitly or implicitly, the features required by the claimed invention. Manfredi does not fill the gaps in Toby."

The testimony of Dr. Burkovski is the only evidence in the record concerning the proper interpretation of the teachings the Toby reference or teachings and suggestions of Toby and Manfredi as understood by one skilled in the art and the Examiner's unsupported statements. If the Examiner seeks to justify her interpretation on the basis of her own knowledge, the Examiner must submit a sworn declaration as required by 37 CFR § 104(d)(2). Otherwise, the rejection of pending claims 1, 4, 5, 7 and 8 under 35 U.S.C. § 102(b) as anticipated by Toby and claim 6 under 35 U.S.C. § 103(a) as being unpatentable over Toby and Manfredi must be withdrawn.

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Respectfully submitted,
REED SMITH LLP



Nanda P.B.A. Kumar
Registration No. 44,853
2500 One Liberty Place
1650 Market Street
Philadelphia, PA 19103-7301
(215) 851-8100
Attorney for Applicant



EXHIBIT A